Attorney Docket No.: 10094.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Sjøholm et al. Confirmation No: 9039

Serial No.: 09/779,323 Group Art Unit: 1652

Filed: February 8, 2001 Examiner: M. Monshipouri

For: Use of Acid Stable Protease in Animal Feed

CERTIFICATE OF FACSIMILE TRANSMISSION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I hereby certify that the attached correspondence comprising:

1. Transmittal of Declaration Under 37 C.F.R. 1.132
2. Declaration Under 37 C.F.R. 1.132

was sent to the United States Patent and Trademark Office by telefax to the attention of Examiner M. Monshipouri, fax number (703) 308-4242.

Respectfully submitted,

Date: August 19, 2003

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TRANSMITTAL OF DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
Washington, DC 20231

Sir:

Applicants recently filed a response to the Advisory Action mailed June 18, 2003. The response was accompanied by a Declaration under 37 C.F.R. 1.132 of Carsten Sjøholm. The Declaration contained two inadvertent errors. In paragraph 1, Mr. Sjøholm's MS degree is in Biochemistry not Chemistry and in paragraph 7, "her" should have been –his—. Attached is a corrected Declaration under 37 C.F.R. 1.132.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: August 19, 2003

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(212) 840-0097

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DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Carsten Sjøholm, do hereby state and declare that

1. I received a MS degree in Biochemistry from the University of Copenhagen in 1978. Since 1981, I have been employed by Novozymes A/S (previously a part of Novo Nordisk A/S), the owner of the above-captioned application. From 1981 – 1990, I was a Research Scientist, and from 1991 until the present, I have been a Science Manager. During the last five years, my responsibilities have involved developing different enzymes for animal feed.

2. I am a named inventor of the above-captioned application and am familiar with the prosecution history thereof.

3. The U.S. Patent and Trademark Office has rejected claims 14 and 21-30 under 35 U.S.C. 103 as being unpatentable in view of Bedford et al. (WO 96/05739) in view of JP 02255081 (Snow-Brand Milk Prod.). Claims 14 and 21-30 are drawn to animal feed additives and compositions comprising, and methods for improving the nutritional value of an animal feed, using a protease which comprises the amino acid sequence of SEQ ID NO: 1, which is an acid-stable protease. I respectfully disagree that the combination of Bedford et al. and JP 02255081 renders these inventions obvious.

4. JP 02255081 discloses a protease produced by *Nocardiopsis* sp. OPC-210 (FERM P-10-508). However, JP 02255081 does not teach or suggest either animal feed

additives and compositions comprising, or methods for improving the nutritional value of an animal feed, using a protease which comprises the amino acid sequence of SEQ ID NO: 1.

5. Bedford et al. disclose the use of various enzymes, including proteases, in animal feed compositions. Bedford et al. disclose at page 25 that the protease may be one of the following commercially available proteases: NEUTRASE™, PURAFECT™, SAVINASE™, MAXACAL™, DURAZYM™ and MAXAPEM™, or a mutant subtilisin described in one of a number of published patent applications. All of the proteases described in Bedford et al. are alkaline proteases and not acid-stable proteases.

The feed additives described in Bedford et al. are said to have an improved (i.e., lower) feed conversion ratio (FCR), which results in more efficient utilization of the feed. However, an improved FCR without a simultaneous increase in body weight is not a significant advantage in practical terms. Furthermore, the results shown in Bedford et al. do not prove Bedford et al.'s allegations of improved FCR. The only experiments using a protease described in Bedford et al. are provided in Examples 2 and 5.

In the experiment described in Example 2, chickens were treated with a control animal feed (with no enzymes), an animal feed designated "Z", which is identical to the control except that it also contains a xylanase, three animal feeds designated "A," "C," and "E", which are identical to Z except that they contain the protease NEUTRASE™, and three animal feeds designated "B," "D" and "F", which are also identical to Z except that they contain a modified *Bacillus amyloliquefaciens* subtilisin protease.

The results, which are provided in Table 4, show that the use of the control animal feed and the animal feed designated Z resulted in a feed conversion ratio of 1.85, the use of the animal feeds designated A, C and E resulted in a feed conversion ratio of 1.85, 1.85 and 1.82 (i.e., two of the animal feeds containing the protease NEUTRASE™ resulted in the same feed conversion ratio as the control animal feed and the animal feed designated Z), and the use of the animal feeds designated B, D and F resulted in a feed conversion ratio of 1.82, which is only a fraction below the FCR obtained with the control animal feed and the animal feed designated Z. It has not been demonstrated that there is a statistical difference between the results obtained using the control animal feed and the animal feed designated Z, on the one hand, and the results obtained using the animal feeds designated A-F, on the other hand. Thus, the results of Example 2 do not prove to one of ordinary skill in the art that the addition of a protease to an animal feed results in an improved feed conversion ratio.

Equally important, it has not been demonstrated that the final body weight was significantly increased using any of the animal feeds designated A-F. The final body weight obtained in the control animal feed and the animal feed designated Z were 2.21 and 2.20 kg, respectively, whereas 2.19 to 2.23 kg were obtained using the animal feeds designated A-F.

Similarly, for the results in Example 5 shown in Table 9, it has not been demonstrated that there is a statistical difference between using a protease-free animal feed and a protease-containing animal feed in FCR or animal body weight. Thus, the results of Example 5 also do not prove to one of ordinary skill in the art that the addition of a protease to an animal feed results in improved performance.

The results in Bedford et al. are consistent with the state of the art. Although there have been suggestions to use proteases in animal feed compositions, proteases that are effective for improving the feed conversion ratio and the nutritional value of an animal feed have not been identified.

6. In contrast, the above-captioned application demonstrates in Example 4 that the protease of SEQ ID NO: 1 (*Nocardiopsis sp.* NRRL 18262 protease) has a statistically and significantly better effect on protein solubilization in the feed, which in turn leads to an improved nutritional value of the feed. These results are surprising and unexpected, especially when considering the thousands of proteases that are known in the art.

7. The undersigned declarant declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize any patent issuing thereon.

Signed this 8 day
of August 2003

Carsten Sjøholm